II. REMARKS

Formal Matters

Claims 1-15 and 20-32 are pending after entry of the amendments set forth herein.

Claims 1-19 were examined and were rejected. Claims 20-27 were withdrawn from consideration.

Claims 4, 5, and 7-15 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claims 4, 5, and 7-15 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: page 10, lines 5-6; and page 19, lines 24-25; page 19, lines 25-27; page 10, lines 10-13; and page 13, lines 16-28. Accordingly, no new matter is added by these amendments.

Claims 16-19 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

The specification is amended to address objections raised in the Office Action. The amendments to the specification are merely editorial in nature, and no new matter is added.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Objections to the specification

The Office Action stated that the disclosure is objected to because of the following informalities: The Office Action stated that the following terms should be spelled out in full at the first instance of use: on page 4, line 15, the terms "MAP," "GRF," "ERPF," and "ERVR"; on page 4, line 21, "RT-PCR" and line 22, "VEGF"; page 14, line 12 "PCR; and line 28 "FGF"; and page 25, line 12, "cGMP."

The abbreviation "VEGF" is spelled out in full at the first instances of use, on page 2, lines 13-14. Accordingly, there is no need to amend the specification to spell out this abbreviation.

Applicants respectfully request amendment of the specification to spell out the abbreviations "MAP," "GRF," "ERPF," "ERVR," "RT-PCR," "FGF," and "cGMP."

Rejection under 35 U.S.C.§112, second paragraph

Claims 1-8, 10-15, 18, and 19 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

Claims 4, 7, 8, 10, 11, 14, 15, 18, and 19

The Office Action stated that claim 4 is indefinite in the recitation of "about 0.1 to 500 μg/kg." The Office Action stated that it is ambiguous as to what is encompassed in these claims. Applicants respectfully traverse the rejection.

The specification states that, in general, a dose is from about 0.1 to 500 μg/kg of body weight. Specification, page 10, lines 5-6; and page 19, lines 24-25. Furthermore, the specification states that in some embodiments, a serum concentration of from about 0.5 to about 50 ng/ml is obtained. Specification, page 19, lines 25-27. The specification further states that the amount of relaxin administered depends on various factors; such factors can readily be determined by a prescribing physician. Specification, page 10, lines 10-13. Accordingly, the claims are clear and need not be amended.

Nevertheless, and solely in the interest of expediting prosecution, claims 4, 7, 8, 10, 11, 14, and 15 are amended to delete the word "about." Claims 18 and 19 are canceled without prejudice to renewal, thereby rendering the rejection of these claims moot.

Claims 5, 7, 8, 11, 15, and 19

The Office Action stated that the recitation of "time sufficient to" in claim 5 is unclear. The Office Action stated that the term "sufficient" is undefined in the specification as to what time point the therapeutic effect can be obtained. Applicants respectfully traverse the rejection.

The specification states that administration of an effective amount of relaxin reduces pulmonary hypertension compared to a control. Specification, page 13, lines 16-28. The specification states that whether pulmonary hypertension is reduced can be determined, e.g., by measuring right ventricular pressure. Specification, page 13, lines 23-25. The specification provides a working example of how to determine whether pulmonary hypertension is reduced. Specification, Example 5. Thus, given the guidance in the specification, those skilled in the art could readily determined whether relaxin was administered for a sufficient period of time.

Nevertheless, and solely in the interest of expediting prosecution, claims 5, 7, 8, 11, and 15 are amended to delete the word "sufficient." Claim 19 is canceled without prejudice to renewal, thereby rendering the rejection of these claims moot.

Claim 11

The Office Action stated that there is insufficient antecedent basis in claim 9, from which claim 11 depends, for "recombinant human relaxin."

Claim 9 is amended to recite "recombinant human relaxin," thereby providing antecedent basis for this term in claim 11.

Claim 12

The Office Action stated that the phrase "increase a parameter associated with" is unclear, and suggested substituting with "increase a factor associated with."

Without conceding as to the correctness of this rejection, claim 12 is amended to recite "increase a factor associated with."

Claim 17

The Office Action stated that claim 17 is vague in the recitation of "an ischemic wound." Claim 17 is canceled without prejudice to renewal, thereby rendering the rejection of this claim moot.

Rejection under 35 U.S.C.§102(a)

Claims 1, 2, 4, 6, 8-11, and 14-19 were rejected under 35 U.S.C.§102(a) as allegedly anticipated by Bigazzi (U.S. Patent No. 5,952,296; "Bigazzi").

Claims 9-15 were rejected under 35 U.S.C.§102(a) as allegedly anticipated by Danielson et al. ((1999) *J. Clin. Invest.* 103:525-533; "Danielson").

Claims 1, 2, 4, 6, 8-11, and 14-19 over Bigazzi

Claims 16-19 are canceled without prejudice to renewal, thereby rendering the rejection of these claims moot.

With respect to claims 1, 2, 4, 6, 8-11, 14, and 15, Bigazzi is not an enabling disclosure, and therefore cannot anticipate the instant invention as claimed.

It is well settled law that a reference must be enabling in order to anticipate a claim. The Federal Circuit has stated in *In re Donahue*, 226 USPQ 619 (Fed. Cir. 1985) that:

> It is well settled that prior art under 35 U.S.C. § 102 (b) must sufficiently describe the claimed invention to have placed the public in possession of it. *In re Sasse*, 629 F.2d 675, 681, 207 U.S.P.Q. (BNA) 107, 111 (CCPA 1980); *In re Samour*, 571 F.2d at 562, 197 U.S.P.Q. at 4; see also *Reading & Bates Construction Co. v. Baker Energy Resources Corp.*, 748 F.2d 645, 651-52, 223 U.S.P.Q. (BNA) 1168, 1173 (Fed. Cir.1984). Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed invention. See *In re LeGrice*, 301 F.2d at 939, 133 U.S.P.Q. at 373-74. Accordingly, even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling. *In re Borst*, 52 C.C.P.A. 1398, 345 F.2d 851, 855, 145 U.S.P.Q. (BNA) 554, 557 (1965), cert. denied, 382 U.S. 973, 83 S. Ct. 537, 15 L. Ed. 2d 465 (1966).

Thus, if a reference is non-enabling for a particular invention, it cannot anticipate that particular invention.

Bigazzi discusses:

1) the effect of relaxin on coronary blood flow in isolated hearts from rats and guinea pigs (Fig. 1A and 1B);
2) the effect of relaxin on coronary blood flow and nitric oxide (NO) release in isolated hearts from animals in the presence of NO-synthase inhibitor or inducer (Fig. 2A and 2B);
3) the effect of relaxin on cGMP levels on aortic smooth muscle cells in *in vitro* culture (Fig.3);
4) the effect of relaxin on histamine release and cytosolic Ca^{2+} release on mast cells *in vitro* (Fig. 4A and 4B);
5) the effect of relaxin on blood flow in the human penis (Fig. 5A-C);
6) the effect of relaxin on platelet aggregation (Fig. 6);

7) the effect of relaxin on thrombane production (Fig. 7);

8) the effect of relaxin on NO production as it relates to platelet aggregation (Fig. 8);

9) the effect of relaxin on platelet aggregation, cGMP, and cytosolic Ca^{2+} (Figs. 9 and 10);

10) the effect of relaxin on ANP secretion (column 7, lines 18-38); and

11) the effect of relaxin on blood osmolality and sodium concentration (column 7, lines 39-45).

There are no data or any other showing of the use of relaxin to treat hypertension, or to increase renal function. None of the data presented in Bigazzi would lead those of ordinary skill in the art to conclude that Bigazzi provided an enabling disclosure for methods of treating hypertension, and methods of increasing renal function. Accordingly, Bigazzi cannot anticipate claims 1, 2, 4, 6, 8-11, 14, and 15.

Claims 9-15; Danielson

Danielson is not available as prior art to the instant application under 35 U.S.C.§102(a). Danielson was published on February 22, 1999. As shown in Exhibit 1, Danielson was not received by libraries until after February 9, 1999. The instant application claims priority to U.S. Provisional Patent Application No. 60/181,408, filed February 9, 2000. Thus, Danielson published less than one year before the priority date of the instant application. Furthermore, as explained below, Danielson is the inventor's own work and is thus not "by another." Accordingly, Danielson is not available as prior art to the instant application under 35 U.S.C.§102(a).

Applicants' disclosure of their own work within one year before the application filing date cannot be used against them under 35 U.S.C.§102(a). Therefore, where the applicants are co-authors of a publication cited against their application, the publication may be removed as a reference by submission of a declaration establishing that the article is describing applicants' own work, *i.e.*, that the publication is not "by another." The courts have found that persons involved only with assay and testing are normally listed as coauthors but are not considered co-inventors.[1] Authorship of an article by itself

[1]In *In re Katz*, 215 USPQ 14 (CCPA 1982), Katz stated in a declaration that the coauthors of the cited publication, Chiorazzi and Eshhar, "were students working under the direction and supervision of the inventor, Dr. David H. Katz." The court held that this declaration, in combination with the fact that the publication was a research paper, was enough to establish Katz as the sole inventor and that the work described in the publication was his own. In research papers, students

does not raise a presumption of inventorship with respect to the subject matter disclosed in the article. Thus, co-authors may not be presumed to be coinventors merely from the fact of co-authorship.

The situation in the present application is similar to that of *In re Katz*. First, the February 22, 1999 date of Danielson is less than one year before the February 9, 2000 priority date of the instant application. Second, the authors listed on Danielson are Lee A. Danielson, O. David Sherwood, and Kirk P. Conrad. Danielson and Sherwood are not co-inventors of the present application. Danielson is not an inventor, as she was working under the direction of Conrad, and did not contribute to the inventive concept. Sherwood is not an inventor, as Sherwood merely contributed materials. Accordingly, Danielson is the inventor Kirk Conrad's own work, and as such is not invention "by another." The Declaration under 37 C.F.R.§1.132 by Dr. Kirk Conrad attests to this fact and is provided herewith as Exhibit 2.

Therefore, in view of the evidence in the form of the Declaration of Kirk Conrad under 37 C.F.R.§1.132, Danielson is not available as prior art under 35 U.S.C.§102 against the present application, as it is derived from the inventors' own work.

Conclusion as to the rejections under 35 U.S.C.§102(a)

Applicants submit that the rejection of claims 1, 2, 4, 6, 8-19 under 35 U.S.C. §102(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§102(e)

Claims 16-19 were rejected under 35 U.S.C.§102(e) as allegedly anticipated by Unemori et al. (U.S. Patent No. 6,211,147; "Unemori")

Claims 16-19 are canceled without prejudice to renewal, thereby rendering the rejection of these claims moot.

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involved only with assay and testing are normally listed as coauthors but are not considered co-inventors.

Applicants submit that the rejection of claims 16-19 under 35 U.S.C. §102(e) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§103

Claims 1, 2, and 4-19 were rejected under 35 U.S.C.§103 as allegedly unpatentable over Bigazzi taken with Unemori. Claims 9-19 were rejected under 35 U.S.C.§103 as allegedly unpatentable over Danielson taken with Unemori.

Claims 1, 2, and 4-19 over Bigazzi taken with Unemori

The Office Action stated: 1) Bigazzi does not explicitly disclose specific relaxin administration routes; 2) Unemori teaches i) a dosage for relaxin; ii) recombinant relaxin; ii) injectable formulation; iv) continuing administration; and v) a serum concentration of relaxin.

Claims 16-19 are canceled without prejudice to renewal, thereby rendering the rejection of these claims moot.

With respect to claims 1, 2, and 4-15, Applicants note that the claim elements for which Unemori is cited are not recited in claims 1, 2, 9, 12, and 13. Applicants presume that inclusion of these claims in this rejection was in error.

As noted above, Bigazzi does not anticipate the instant invention as claimed. A disclosure of i) a dosage for relaxin; ii) recombinant relaxin; ii) injectable formulation; iv) continuing administration; and v) a serum concentration of relaxin, does not render the instant claims obvious.

Claims 9-19 over Danielson taken with Unemori

Claims 16-19 are canceled without prejudice to renewal, thereby rendering the rejection of these claims moot.

As discussed above, Danielson is not available as prior art under 35 U.S.C.§102 to the instant application. Accordingly, Danielson cannot render instant claims 9-15 obvious.

Conclusion as to the rejections under 35 U.S.C.§103

Applicants submit that the rejection of claims 1, 2, and 4-19 under 35 U.S.C. §103 has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number CONN001.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: Feb. 21, 2003

By: _____
Paula A. Borden
Registration No. 42,344

BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

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